CLAIMS

[Claim(s)]

[Claim 1] The culture approach of the cell lump characterize by make it stabilize in the condition of produce the stream of the 2-way which intersect perpendicularly mutually in the cultural tank which cultivate a cell lump , the spherical closing loop formation of a uniform elementary stream be form near the core of a cultural tank of the stream of the 2-way which intersect perpendicularly mutually , lose according to it most effects of the gravity to the cell lump which float near the core of a cultural tank , and hang inside in culture medium .

[Claim 2] In the culture medium in the cultural tank which cultivates a cell lump According to the stream of the 2-way which intersects perpendicularly mutually, the flow of the direction of slant which goes to a specific field as a whole is produced. The stream, The culture approach of the cell lump according to claim 1 characterized by always maintaining fresh the culture medium which replaces the culture medium of each class gradually and contacts a cell lump, making the circulating flow of an inside-and-outside multilayer form making the stream which turned to other fields join.

[Claim 3] It is the bioreactor characterized by being the bioreactor equipped with the cultural tank with which culture medium and gas are supplied from the exterior, and for a cultural tank being a container which holds the cell lump which should cultivate, and being that by which a rotation drive is carried out by making into the center of rotation biaxial [of the rectangular coordinates which intersect perpendicularly mutually], respectively.

[Claim 4] They are a cultural tank and the bioreactor which has combination with an envelope. A cultural tank It is the container which holds the cell lump which should cultivate. An envelope It is the container which holds a cultural tank, and a cultural tank and an envelope are mutually open for free passage, and circulation of culture medium is free. The revolving-shaft alignment of an envelope, It intersects perpendicularly with the revolving-shaft alignment of a cultural tank, and culture medium and gas are supplied from the outside in an envelope. A cultural tank The bioreactor characterized by being that in which a rotation drive is carried out by the driving source which is held still more pivotable in an one direction in the envelope by which a rotation drive is carried out, and an envelope and really rotates.

[Claim 5] It is the bioreactor according to claim 3 or 4 characterized by the fluid which it has a nozzle, and a nozzle blows off a fluid, rotating to an envelope and one, and a cultural tank has an impeller, and blew off from the nozzle being what it collides [what] with an impeller and rotates a cultural tank.

[Claim 6] The culture medium which the feed pipe for supply of culture medium was connected to the nozzle, and blew off from the nozzle is a bioreactor according to claim 4 or 5 characterized by being a thing used as the fluid made to rotate a cultural tank.

[Claim 7] The feed pipe which an envelope is held at a level posture, a rotation drive is carried out in an one direction, a cultural tank is held pivotable in the direction which crosses the drum section of the barrel of an envelope by pivot bearing, and culture medium supplies is a bioreactor according to claim 6 characterized by being what it is piped on the same axial center as the revolving shaft of an envelope, and a nozzle is combined with a feed pipe pivotable, and an envelope and really rotates.

[Translation done.]

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to the bioreactor used for culture of a cell lump's culture approach and a cell lump.
[0002]
[Description of the Prior Art] A bioreactor is equipment which cultivates the cell lump, making the cell lump of a "living thing" float in culture medium. Culture medium is culture fluid grown up per cell of a living thing. The work which stimulates fission of a cell or assists a with growth of a cell lump by making this culture fluid contain the nutrient which needs a cell for growth, gas, for example, carbon dioxide gas, oxygen, etc. can be obtained.
[0003] It faces making it grow up, making a cell lump float to the culture medium with which it was filled up in the cultural tank, and making culture medium flow continuously hydrodynamically is searched for. That is, it is proved by making culture medium flow continuously within a cultural tank hydrodynamically that the gas to condensation, cell agglutination lump, and explant of cells and the efficiency of materials handling of the training matter increase dramatically.
[0004]
[Problem(s) to be Solved by the Invention] it was alike and the conventional bioreactor was cylindrical, the constraint on structure will be received from the need of connecting piping for supply of culture medium to the rotating cultural tank, for the appropriate method which supplies culture medium in a cultural tank from the exterior with gas, and the thing of a 1 shaft rotary system which rotates the structure attached in the revolving shaft which a cultural tank rotates in an orientation, i.e., one shaft, as the center of rotation was almost the case.
[0005] However, only by rotating a cultural tank with one shaft Since the inclination which regularity arises in a motion of the culture medium within a cultural tank, divides to it, diffuses a revolving shaft in the direction of a right angle, and goes is strong, There was a trouble that the wastes which culture medium could not be made to fully flow within a cultural tank, but liquid deteriorated for this reason, and were produced in liquid were unremovable, and there was a fault that only comparatively short time amount could cultivate.
[0006] It is very important to make the space (the so-called simulation gravity-free space) where the cell lump which should cultivate is hardly influenced of gravity in the latest researches on a biotechnology technique, such as culture of a cell lump.
[0007] The purpose of this invention is to offer the approach of rotating a cultural tank in the biaxial direction of rectangular coordinates, and cultivating a cell lump, and a bioreactor, supplying culture medium from the exterior.
[0008]
[Means for Solving the Problem] In the culture approach of the cell lump according to this invention in order to attain the above-mentioned purpose According to the stream of the 2-way which is made to produce the stream of the 2-way which intersects perpendicularly mutually, and intersects perpendicularly mutually in the cultural tank which cultivates a cell lump The spherical closing loop formation of a uniform elementary stream is formed near the core of a cultural tank, and you lose most effects of the gravity to the cell lump which floats near the core of a cultural tank, and make it stabilized in the condition of hanging inside in culture medium.
[0009] Moreover, the flow of the direction of slant which goes to a specific field as a whole is produced according to the stream of the 2-way which intersects perpendicularly with the culture medium in the cultural tank which cultivates a cell lump mutually, making the circulating flow of an inside-and-outside multilayer form making the stream and the stream which turned to other fields join, the culture medium of each class is replaced gradually and the culture medium in contact with a cell lump is always maintained fresh.
[0010] Moreover, it is the bioreactor equipped with the cultural tank with which culture medium and gas are supplied from the exterior in the bioreactor by this invention, and a cultural tank is a container which holds the cell lump which should cultivate, it makes biaxial [of the rectangular coordinates which intersect perpendicularly mutually] the center of rotation, respectively, and a rotation drive is carried out.
[0011] They are a cultural tank and the bioreactor which has combination with an envelope. Moreover, a cultural tank It is the container which holds the cell lump which should cultivate. An envelope It is the container which holds a cultural tank, and a cultural tank and an envelope are mutually open for free passage, and circulation of culture medium is free. The revolving-shaft alignment of an envelope, It intersects perpendicularly and culture medium and gas are supplied from the outside in an envelope, a cultural tank is held still more pivotable in the envelope by which a rotation drive is carried out in an one direction, and the rotation drive of the revolving-shaft alignment of a cultural

tank is carried out by the driving source which an envelope and really rotates.
[0012] Moreover, it has a nozzle, a nozzle blows off a fluid, rotating to an envelope and one, a cultural tank has an impeller, and the fluid which blew off from the nozzle collides with an impeller, and rotates a cultural tank.
[0013] Moreover, the feed pipe for supply of culture medium is connected to a nozzle, and the culture medium which blew off from the nozzle serves as a fluid made to rotate a cultural tank.
[0014] Moreover, the feed pipe which an envelope is held at a level posture, a rotation drive is carried out in an one direction, a cultural tank is held pivotable in the direction which crosses the drum section of the barrel of an envelope by pivot bearing, and culture medium supplies is piped on the same axial center as the revolving shaft of an envelope, and it is combined with a feed pipe pivotable and it an envelope and really rotates a nozzle.
[0015]
[Embodiment of the Invention] Drawing explains the gestalt of operation of the bioreactor by this invention below. In drawing 1 , the bioreactor 1 by this invention is equipped with the cultural tank 2 with which culture medium and gas are supplied from the exterior, a cultural tank 2 makes biaxial [of the rectangular coordinates which intersect perpendicularly mutually] the center of rotation, respectively, and a rotation drive is carried out.
[0016] The bioreactor 1 by this invention has the combination of a cultural tank 2 and an envelope 3. A cultural tank 2 is a container which contains the cell lump which should cultivate, and an envelope 3 is a container which contains a cultural tank 2. A cultural tank 2 and an envelope 3 are mutually open for free passage, culture medium can circulate freely mutually between a cultural tank 2 and an envelope 3, and flows into a cultural tank 2 from an envelope 3, or the culture medium in a cultural tank 2 flows out in an envelope 3 conversely.
[0017] It fills up with culture medium C (it is also called the liquid and culture medium containing a nutrient required for growth of a cell) in the thermostat 5 kept warm by constant temperature within the incubator 4. The culture medium C in a thermostat 5 is pumped out by feed pipe 7A with a metering pump 6, filters culture medium C via a filter 8, subsequently blows off from a nozzle 9, and is supplied in an envelope 3. On the other hand, the gas holder 10 filled up with gas is put in an incubator 4, and the gas in a gas holder 10 is controlled by fixed temperature, has the supply pressure of the gas supplied from the outside, at the time of the need, it is supplied in a thermostat 5 and mixed by the culture medium C in a thermostat 5. Gas is gas for making a cell lump survive and proliferating a cell, and is gas containing CO2:2.5%, N2:20%, and O2:20%.
[0018] Therefore, when gas is supplied in a thermostat 5, culture medium C is supplied in an envelope 3 in the form of a vapor-liquid interflow object. In addition, an incubator 4 has a heater 11 in a tub, a heater 11 is controlled by the temperature selector 12, and the water in an incubator 4 is maintained at constant temperature (for example, 37**0.1 degrees C), the stirring pump 13 stirring. The gas which drain pipe 7B and exhaust gas pipe 7C were connected to the envelope 3, and was sent in in the envelope 3 is emitted to the open air through exhaust gas pipe 7C.
[0019] Moreover, drain pipe 7B is connected to a thermostat 5, and the culture medium C which flowed out of the inside of an envelope 3 removes wastes, and is returned in the after [processing] thermostat 5. In this operation gestalt, the injection pressure of the culture medium (vapor-liquid mixing culture medium) spouted from a nozzle 9 is used for the rotation driving source of a cultural tank 2 so that it may mention later.
[0020] In drawing 2 (a), an envelope 3 is the barrel with which both ends were taken up, it is held pivotable through bearing 14 at a posture level to a machine frame F, and the pulley 16 fixed to the end plate 15 which plugs up one opening of a barrel, and the pulley 18 attached in the revolving shaft of a motor 17 are directly linked with the endless belt 19.
[0021] Therefore, an envelope 3 rotates to an one direction by the drive of a motor 17 by using the 1st shaft (horizontal axis; the X-axis being set as this) of rectangular coordinates as a revolving-shaft alignment. A cultural tank 2 is supported to the pivot bearing 20 prepared for making it face the drum section of the barrel of an envelope 3, and the 2nd shaft (vertical axes: set a Y-axis as this) which crosses the drum section of the barrel of an envelope 3 is held pivotable as a revolving-shaft alignment.
[0022] That is, opening of the free passage hole 22 which makes the inside and outside of a cultural tank 2 open for free passage is carried out, to both the cover plates 21, it flows in a cultural tank 2 from the free passage hole 22 through a filter 27, and the interior is filled, it is the barrel which has the cover plate 21 with which a cultural tank 2 opens and closes a cultural tank 2 in drawing 3 to both ends, and it interchanges [the culture medium C supplied in the envelope 3 flows out of the free passage hole 22 in an envelope 3 conversely, and] to them. The pivot 23 which said pivot bearing 20 is made to support is attached in the external surface of both cover plates. The pivot 23 is supported pivotable to the bearing prepared for making it face the drum section inside of the barrel of an envelope 3. a part of barrel of a cultural tank 2 -- the impeller 24 is attached in the peripheral surface.
[0023] The end plate 15 which plugs up one opening of an envelope 3 is a rounded-end plate directly linked with the pulley 16. Feed pipe 7A which supplies culture medium is piped by the revolving-shaft alignment and this alignment of the rounded-end plate 15. A nozzle 9 Feed pipe 7A is a thing which was combined mutually pivotable, and could shift the tip from the revolving-shaft alignment, has been arranged with the crookedness posture towards the impeller 24 of a cultural tank 2, crossed the barrel drum section of an envelope 3 as shown in drawing 2 (b), and was attached in the barrel wall and which supports and is supported by 26. In addition, drain pipe 7B and exhaust gas pipe 7C are supported by the bush 25 fixed to the machine frame F, and opening is carried out into the envelope 3. In addition, the end plate 15 is supported by the periphery of a bush 25 pivotable.
[0024] In this invention, the cell lump which should cultivate is held in a cultural tank 2. A cultural tank 2 Set in an envelope 3 and the inside of an envelope 3 and a cultural tank 2 is filled with culture medium. Mix the culture medium C in the thermostat 5 furthermore pumped out with the metering pump 6, and the gas with which it filled up in the

gas holder 10, and the vapor-liquid mixing culture medium is made to flow into feed pipe 7A, and culture of a cell lump is started, blowing off from a nozzle 9 in an envelope 3.

[0025] On the occasion of culture of a cell lump, an envelope 3 is gently rotated by using a horizontal axis (X-axis) as a revolving-shaft alignment by the rotation drive of a motor 17. The culture medium C which the nozzle 9 blew off culture medium C, rotating to an envelope 3 and one, and blew off from the nozzle 9 collides with an impeller 24. A cultural tank 2 It supports to the pivot bearing 20 of an envelope 3, and they are gently rotated in the culture medium of an envelope 3, using vertical axes (Y-axis) as a revolving-shaft alignment. In a cultural tank 2 The stream of the 2-way which intersects perpendicularly mutually arises, and the spherical closing loop formation of an elementary stream with the stream of the 2-way which intersects perpendicularly mutually uniform near the core of a cultural tank is formed.

[0026] The situation of the stream of the culture medium produced in a cultural tank 2 is explained using drawing 4 . When an envelope 3 rotates focusing on the X-axis and a cultural tank 2 rotates focusing on a Y-axis to coincidence in drawing 4 (a), to the culture medium C in a cultural tank 2 The force of a Z direction shown in drawing is received as resultant force with the force of the direction of X, and the force of the direction of Y. In a specific field and this example, as a whole on drawing The flow of the direction of slant which goes to the 1st field arises from the 4th field. With the stream In other field and this example, the stream which turned to the 2nd field and the 3rd field joins, and it becomes circulating flow. Fundamentally As shown in drawing 4 (b), a multiplex laminar flow forms a spherical closing loop formation, respectively. A surface current Fo, Although the stream of a concentric circle is drawn without rapid turbulence arising with the flow between the inner layer styles Fi, the culture medium of each class interchanges gradually with a flow of culture medium, and the culture medium in contact with a cell lump is always kept fresh.

[0027] Consequently, the gravity concerning the cell lump which floats the inside of a cultural tank 2 is mitigated by rotation of the X-axis and a Y-axis, a false gravity-free space is formed in a cultural tank 2, and it is hardly influenced of gravity, but the cell lump which floats near the core in a cultural tank 2 will be in the condition of hanging inside in culture medium C, and will be stabilized.

[0028] As mentioned above, in an operation gestalt, although the example using the injection pressure of the culture medium (vapor-liquid mixing culture medium) C made to blow off from a nozzle 9 as a source of power which rotates a cultural tank 2 was explained, of course, it is possible not only culture medium but to be able to use fluids, such as other circulating water, air, or gas, for the power for rotating a cultural tank, and to drive mechanically further using frictional force.

[0029] However, it is more desirable for using magnetic force and electric force for the drive of a cultural tank to avoid, although the drive of a cultural tank is possible even if it uses magnetic force and electric force since the drive by coupling of the MAG and the electrical and electric equipment has the opinion of having a bad influence on a cell. The rotation drive of the driving source of an envelope can also be carried out not only using a motor but using pneumatic pressure or gas pressure.

[0030]

[Effect of the Invention] When based on this invention as mentioned above, in order to carry out a rotation drive from the exterior, using as the center of rotation biaxial [of the rectangular coordinates which intersect perpendicularly mutually the cultural tank with which culture medium and gas are supplied], respectively, In order that the spherical closing loop formation of a uniform elementary stream may form near the core of a cultural tank according to the stream of the 2-way which is made to produce the stream of the 2-way which intersects perpendicularly mutually, and intersects perpendicularly mutually in the cultural tank which cultivates a cell lump, You can lose most effects of the gravity to the cell lump which floats near the core of a cultural tank, and can make it stabilized in the condition of hanging inside in culture medium.

[0031] Moreover, using the combination of a cultural tank and an envelope, a cultural tank and an envelope can be opened for free passage mutually and can write circulation of culture medium as it is free, and the stream of the 2-way which intersects perpendicularly mutually [it is reasonable and] in a cultural tank with the combination of the revolving-shaft alignment of an envelope and the revolving-shaft alignment of a cultural tank can be produced. Furthermore, culture medium or gas can be made to be able to blow off from a nozzle to a cultural tank, and it can be made to rotate a cultural tank further by preparing an impeller within the envelope which rotates with the injection pressure.

[Translation done.]

* NOTICES *

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TECHNICAL FIELD

[Field of the Invention] This invention relates to the bioreactor used for culture of a cell lump's culture approach and a cell lump.

[Translation done.]

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PRIOR ART

[Description of the Prior Art] A bioreactor is equipment which cultivates the cell lump, making the cell lump of a "living thing" float in culture medium. Culture medium is culture fluid grown up per cell of a living thing. The work which stimulates fission of a cell or assists a with growth of a cell lump by making this culture fluid contain the nutrient which needs a cell for growth, gas, for example, carbon dioxide gas, oxygen, etc. can be obtained.
[0003] It faces making it grow up, making a cell lump float to the culture medium with which it was filled up in the cultural tank, and making culture medium flow continuously hydrodynamically is searched for. That is, it is proved by making culture medium flow continuously within a cultural tank hydrodynamically that the gas to condensation, cell agglutination lump, and explant of cells and the efficiency of materials handling of the training matter increase dramatically.

[Translation done.]

EFFECT OF THE INVENTION

[Effect of the Invention] When based on this invention as mentioned above, in order to carry out a rotation drive from the exterior, using as the center of rotation biaxial [of the rectangular coordinates which intersect perpendicularly mutually the cultural tank with which culture medium and gas are supplied], respectively, In order that the spherical closing loop formation of a uniform elementary stream may form near the core of a cultural tank according to the stream of the 2-way which is made to produce the stream of the 2-way which intersects perpendicularly mutually, and intersects perpendicularly mutually in the cultural tank which cultivates a cell lump, You can lose most effects of the gravity to the cell lump which floats near the core of a cultural tank, and can make it stabilized in the condition of hanging inside in culture medium.
[0031] Moreover, using the combination of a cultural tank and an envelope, a cultural tank and an envelope can be opened for free passage mutually and can write circulation of culture medium as it is free, and the stream of the 2-way which intersects perpendicularly mutually [it is reasonable and] in a cultural tank with the combination of the revolving-shaft alignment of an envelope and the revolving-shaft alignment of a cultural tank can be produced. Furthermore, culture medium or gas can be made to be able to blow off from a nozzle to a cultural tank, and it can be made to rotate a cultural tank further by preparing an impeller within the envelope which rotates with the injection pressure.

[Translation done.]

TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] it was alike and the conventional bioreactor was cylindrical, the constraint on structure will be received from the need of connecting piping for supply of culture medium to the rotating cultural tank, for the appropriate method which supplies culture medium in a cultural tank from the exterior with gas, and the thing of a 1 shaft rotary system which rotates the structure attached in the revolving shaft which a cultural tank rotates in an orientation, i.e., one shaft, as the center of rotation was almost the case.

[0005] However, only by rotating a cultural tank with one shaft Since the inclination which regularity arises in a motion of the culture medium within a cultural tank, divides to it, diffuses a revolving shaft in the direction of a right angle, and goes is strong, There was a trouble that the wastes which culture medium could not be made to fully flow within a cultural tank, but liquid deteriorated for this reason, and were produced in liquid were unremovable, and there was a fault that only comparatively short time amount could cultivate.

[0006] It is very important to make the space (the so-called simulation gravity-free space) where the cell lump which should cultivate is hardly influenced of gravity in the latest researches on a biotechnology technique, such as culture of a cell lump.

[0007] The purpose of this invention is to offer the approach of rotating a cultural tank in the biaxial direction of rectangular coordinates, and cultivating a cell lump, and a bioreactor, supplying culture medium from the exterior.

[0008]

[Translation done.]

MEANS

[Means for Solving the Problem] In the culture approach of the cell lump according to this invention in order to attain the above-mentioned purpose According to the stream of the 2-way which is made to produce the stream of the 2-way which intersects perpendicularly mutually, and intersects perpendicularly mutually in the cultural tank which cultivates a cell lump The spherical closing loop formation of a uniform elementary stream is formed near the core of a cultural tank, and you lose most effects of the gravity to the cell lump which floats near the core of a cultural tank, and make it stabilized in the condition of hanging inside in culture medium.
[0009] Moreover, the flow of the direction of slant which goes to a specific field as a whole is produced according to the stream of the 2-way which intersects perpendicularly with the culture medium in the cultural tank which cultivates a cell lump mutually, making the circulating flow of an inside-and-outside multilayer form making the stream and the stream which turned to other fields join, the culture medium of each class is replaced gradually and the culture medium in contact with a cell lump is always maintained fresh.
[0010] Moreover, it is the bioreactor equipped with the cultural tank with which culture medium and gas are supplied from the exterior in the bioreactor by this invention, and a cultural tank is a container which holds the cell lump which should cultivate, it makes biaxial [of the rectangular coordinates which intersect perpendicularly mutually] the center of rotation, respectively, and a rotation drive is carried out.
[0011] They are a cultural tank and the bioreactor which has combination with an envelope. Moreover, a cultural tank It is the container which holds the cell lump which should cultivate. An envelope It is the container which holds a cultural tank, and a cultural tank and an envelope are mutually open for free passage, and circulation of culture medium is free. The revolving-shaft alignment of an envelope, It intersects perpendicularly and culture medium and gas are supplied from the outside in an envelope, a cultural tank is held still more pivotable in the envelope by which a rotation drive is carried out in an one direction, and the rotation drive of the revolving-shaft alignment of a cultural tank is carried out by the driving source which an envelope and really rotates.
[0012] Moreover, it has a nozzle, a nozzle blows off a fluid, rotating to an envelope and one, a cultural tank has an impeller, and the fluid which blew off from the nozzle collides with an impeller, and rotates a cultural tank.
[0013] Moreover, the feed pipe for supply of culture medium is connected to a nozzle, and the culture medium which blew off from the nozzle serves as a fluid made to rotate a cultural tank.
[0014] Moreover, the feed pipe which an envelope is held at a level posture, a rotation drive is carried out in an one direction, a cultural tank is held pivotable in the direction which crosses the drum section of the barrel of an envelope by pivot bearing, and culture medium supplies is piped on the same axial center as the revolving shaft of an envelope, and it is combined with a feed pipe pivotable and it an envelope and really rotates a nozzle.
[0015]
[Embodiment of the Invention] Drawing explains the gestalt of operation of the bioreactor by this invention below. In drawing 1 , the bioreactor 1 by this invention is equipped with the cultural tank 2 with which culture medium and gas are supplied from the exterior, a cultural tank 2 makes biaxial [of the rectangular coordinates which intersect perpendicularly mutually] the center of rotation, respectively, and a rotation drive is carried out.
[0016] The bioreactor 1 by this invention has the combination of a cultural tank 2 and an envelope 3. A cultural tank 2 is a container which contains the cell lump which should cultivate, and an envelope 3 is a container which contains a cultural tank 2. A cultural tank 2 and an envelope 3 are mutually open for free passage, culture medium can circulate freely mutually between a cultural tank 2 and an envelope 3, and flows into a cultural tank 2 from an envelope 3, or the culture medium in a cultural tank 2 flows out in an envelope 3 conversely.
[0017] It fills up with culture medium C (it is also called the liquid and culture medium containing a nutrient required for growth of a cell) in the thermostat 5 kept warm by constant temperature within the incubator 4. The culture medium C in a thermostat 5 is pumped out by feed pipe 7A with a metering pump 6, filters culture medium C via a filter 8, subsequently blows off from a nozzle 9, and is supplied in an envelope 3. On the other hand, the gas holder 10 filled up with gas is put in an incubator 4, and the gas in a gas holder 10 is controlled by fixed temperature, has the supply pressure of the gas supplied from the outside, at the time of the need, it is supplied in a thermostat 5 and mixed by the culture medium C in a thermostat 5. Gas is gas for making a cell lump survive and proliferating a cell, and is gas containing CO2:2.5%, N2:20%, and O2:20%.
[0018] Therefore, when gas is supplied in a thermostat 5, culture medium C is supplied in an envelope 3 in the form of a vapor-liquid interflow object. In addition, an incubator 4 has a heater 11 in a tub, a heater 11 is controlled by the temperature selector 12, and the water in an incubator 4 is maintained at constant temperature (for example, 37**0.1 degrees C), the stirring pump 13 stirring. The gas which drain pipe 7B and exhaust gas pipe 7C were connected to

the envelope 3, and was sent in in the envelope 3 is emitted to the open air through exhaust gas pipe 7C.
[0019] Moreover, drain pipe 7B is connected to a thermostat 5, and the culture medium C which flowed out of the inside of an envelope 3 removes wastes, and is returned in the after [processing] thermostat 5. In this operation gestalt, the injection pressure of the culture medium (vapor-liquid mixing culture medium) spouted from a nozzle 9 is used for the rotation driving source of a cultural tank 2 so that it may mention later.
[0020] In drawing 2 (a), an envelope 3 is the barrel with which both ends were taken up, it is held pivotable through bearing 14 at a posture level to a machine frame F, and the pulley 16 fixed to the end plate 15 which plugs up one opening of a barrel, and the pulley 18 attached in the revolving shaft of a motor 17 are directly linked with the endless belt 19.
[0021] Therefore, an envelope 3 rotates to an one direction by the drive of a motor 17 by using the 1st shaft (horizontal axis; the X-axis being set as this) of rectangular coordinates as a revolving-shaft alignment. A cultural tank 2 is supported to the pivot bearing 20 prepared for making it face the drum section of the barrel of an envelope 3, and the 2nd shaft (vertical axes: set a Y-axis as this) which crosses the drum section of the barrel of an envelope 3 is held pivotable as a revolving-shaft alignment.
[0022] That is, opening of the free passage hole 22 which makes the inside and outside of a cultural tank 2 open for free passage is carried out, to both the cover plates 21, it flows in a cultural tank 2 from the free passage hole 22 through a filter 27, and the interior is filled, it is the barrel which has the cover plate 21 with which a cultural tank 2 opens and closes a cultural tank 2 in drawing 3 to both ends, and it interchanges [the culture medium C supplied in the envelope 3 flows out of the free passage hole 22 in an envelope 3 conversely, and] to them. The pivot 23 which said pivot bearing 20 is made to support is attached in the external surface of both cover plates. The pivot 23 is supported pivotable to the bearing prepared for making it face the drum section inside of the barrel of an envelope 3. a part of barrel of a cultural tank 2 -- the impeller 24 is attached in the peripheral surface.
[0023] The end plate 15 which plugs up one opening of an envelope 3 is a rounded-end plate directly linked with the pulley 16. Feed pipe 7A which supplies culture medium is piped by the revolving-shaft alignment and this alignment of the rounded-end plate 15. A nozzle 9 Feed pipe 7A is a thing which was combined mutually pivotable, and could shift the tip from the revolving-shaft alignment, has been arranged with the crookedness posture towards the impeller 24 of a cultural tank 2, crossed the barrel drum section of an envelope 3 as shown in drawing 2 (b), and was attached in the barrel wall and which supports and is supported by 26. In addition, drain pipe 7B and exhaust gas pipe 7C are supported by the bush 25 fixed to the machine frame F, and opening is carried out into the envelope 3. In addition, the end plate 15 is supported by the periphery of a bush 25 pivotable.
[0024] In this invention, the cell lump which should cultivate is held in a cultural tank 2. A cultural tank 2 Set in an envelope 3 and the inside of an envelope 3 and a cultural tank 2 is filled with culture medium. Mix the culture medium C in the thermostat 5 furthermore pumped out with the metering pump 6, and the gas with which it filled up in the gas holder 10, and the vapor-liquid mixing culture medium is made to flow into feed pipe 7A, and culture of a cell lump is started, blowing off from a nozzle 9 in an envelope 3.
[0025] On the occasion of culture of a cell lump, an envelope 3 is gently rotated by using a horizontal axis (X-axis) as a revolving-shaft alignment by the rotation drive of a motor 17. The culture medium C which the nozzle 9 blew off culture medium C, rotating to an envelope 3 and one, and blew off from the nozzle 9 collides with an impeller 24. A cultural tank 2 It supports to the pivot bearing 20 of an envelope 3, and they are gently rotated in the culture medium of an envelope 3, using vertical axes (Y-axis) as a revolving-shaft alignment. In a cultural tank 2 The stream of the 2-way which intersects perpendicularly mutually arises, and the spherical closing loop formation of an elementary stream with the stream of the 2-way which intersects perpendicularly mutually uniform near the core of a cultural tank is formed.
[0026] The situation of the stream of the culture medium produced in a cultural tank 2 is explained using drawing 4 . When an envelope 3 rotates focusing on the X-axis and a cultural tank 2 rotates focusing on a Y-axis to coincidence in drawing 4 (a), to the culture medium C in a cultural tank 2 The force of a Z direction shown in drawing is received as resultant force with the force of the direction of X, and the force of the direction of Y. In a specific field and this example, as a whole on drawing The flow of the direction of slant which goes to the 1st field arises from the 4th field. With the stream In other field and this example, the stream which turned to the 2nd field and the 3rd field joins, and it becomes circulating flow. Fundamentally As shown in drawing 4 (b), a multiplex laminar flow forms a spherical closing loop formation, respectively. A surface current Fo, Although the stream of a concentric circle is drawn without rapid turbulence arising with the flow between the inner layer styles Fi, the culture medium of each class interchanges gradually with a flow of culture medium, and the culture medium in contact with a cell lump is always kept fresh.
[0027] Consequently, the gravity concerning the cell lump which floats the inside of a cultural tank 2 is mitigated by rotation of the X-axis and a Y-axis, a false gravity-free space is formed in a cultural tank 2, and it is hardly influenced of gravity, but the cell lump which floats near the core in a cultural tank 2 will be in the condition of hanging inside in culture medium C, and will be stabilized.
[0028] As mentioned above, in an operation gestalt, although the example using the injection pressure of the culture medium (vapor-liquid mixing culture medium) C made to blow off from a nozzle 9 as a source of power which rotates a cultural tank 2 was explained, of course, it is possible not only culture medium but to be able to use fluids, such as other circulating water, air, or gas, for the power for rotating a cultural tank, and to drive mechanically further using frictional force.
[0029] However, it is more desirable for using magnetic force and electric force for the drive of a cultural tank to avoid, although the drive of a cultural tank is possible even if it uses magnetic force and electric force since the drive

by coupling of the MAG and the electrical and electric equipment has the opinion of having a bad influence on a cell. The rotation drive of the driving source of an envelope can also be carried out not only using a motor but using pneumatic pressure or gas pressure.

[Translation done.]

DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] It is drawing showing the configuration of the whole bioreactor.
[Drawing 2] The cross-section side elevation in which (a) shows the structure of a bioreactor, and (b) are the B-B line sectional views of (a).
[Drawing 3] It is the expanded sectional view of a cultural tank.
[Drawing 4] Drawing showing typically the direction of the circulating water style which produces (a) in a cultural tank, and (b) are drawings showing signs that a surface current and a inner layer style are formed concentrically.
[Description of Notations]
1 Bioreactor
2 Cultural Tank
3 Envelope
5 Thermostat
7A Feed pipe
7B Drain pipe
7C Exhaust gas pipe
9 Nozzle
14 Bearing
15 End Plate
16 18 Pulley
17 Motor
20 Pivot Bearing
22 Free Passage Hole
24 Impeller
25 Bush
26 Support
27 Filter

[Translation done.]

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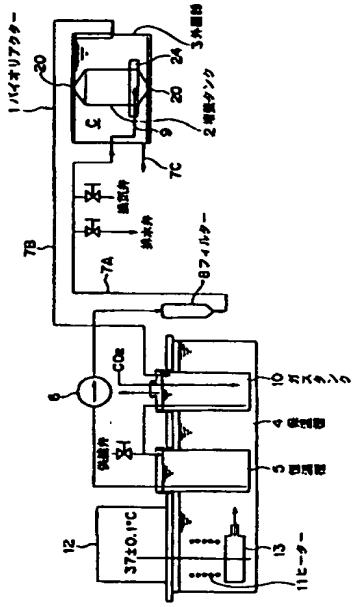
最終頁に続く

(54)【発明の名称】　細胞塊の培養方法およびバイオリアクター

(57)【要約】
【課題】　外部から培養液を供給しつつ培養タンクを直交座標の２軸方向に回転させて細胞塊の培養を行なう。
【解決手段】　バイオリアクター１は、培養タンク２と、外囲器３との組合せを有している。培養タンク２は、培養すべき細胞塊を収容する容器であり、外囲器３は、培養タンク２を収容する容器である。培養タンク２と、外囲器３とは、互いに培養液の流通が自在であり、培養液およびガスは、外囲器３内に外部から供給される。外囲器３は、直交座標の第１軸を回転軸心として一方向に回転駆動され、培養タンク２は、外囲器３の筒体の胴部を横切る第２軸を回転軸心として回転駆動される。この結果、培養タンク２内には、互いに直交する２方向の水流が生じ、この水流によって、培養タンク２の中心付近には均一な流線の球状閉鎖ループが形成され、培養タンク２の中心付近に浮遊する細胞塊への重力の影響は殆どなく、培養液中で細胞塊は中吊りの状態で安定する。



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【特許請求の範囲】

【請求項１】　細胞塊を培養する培養タンク内に、互いに直交する２方向の水流を生じさせ、互いに直交する２方向の水流によって、培養タンクの中心付近には均一な流線の球状閉鎖ループが形成され、培養タンクの中心付近に浮遊する細胞塊への重力の影響を殆どなくし、培養液中で中吊りの状態で安定させることを特徴とする細胞塊の培養方法。

【請求項２】　細胞塊を培養する培養タンク内の培養液には、互いに直交する２方向の水流によって、全体として特定の領域に向かう斜め方向の流れを生じさせ、その水流と、他の領域に回り込んだ水流とを合流させつつ内外多層の循環流を形成させつつ、徐々に各層の培養液を入れ替えて細胞塊に接触する培養液を常に新鮮に保たせることを特徴とする請求項１に記載の細胞塊の培養方法。

【請求項３】　外部から培養液およびガスが供給される培養タンクを備えたバイオリアクターであって、

培養タンクは、培養すべき細胞塊を収容する容器であり、互いに直交する直角座標の２軸をそれぞれ回転中心として回転駆動されるものであることを特徴とするバイオリアクター。

【請求項４】　培養タンクと、外囲器との組合わせを有するバイオリアクターであって、

培養タンクは、培養すべき細胞塊を収容する容器であり、

外囲器は、培養タンクを収容する容器であり、

培養タンクと、外囲器とは互いに連通して培養液の流通は自在であり、外囲器の回転軸心と、培養タンクの回転軸心とは直交し、培養液およびガスは外囲器内に外部から供給され、

培養タンクは、一方向に回転駆動される外囲器内にさらに回転可能に保持され、外囲器と一体回転する駆動源によって回転駆動されるものであることを特徴とするバイオリアクター。

【請求項５】　ノズルを有し、

ノズルは、外囲器と一体に回転しつつ流体を噴出し、

培養タンクは、羽根車を有し、

ノズルから噴出した流体は羽根車に衝突して培養タンクを回転させるものであることを特徴とする請求項３または４に記載のバイオリアクター。

【請求項６】　培養液の供給用の給水管はノズルに接続され、ノズルより噴出した培養液は、培養タンクを回転させる流体となるものであることを特徴とする請求項４または５に記載のバイオリアクター。

【請求項７】　外囲器は、水平の姿勢に保持されて一方向に回転駆動され、

培養タンクは、ピボット軸受によって外囲器の筒体の胴部を横切る方向に回転可能に保持され、

培養液の供給する給水管は、外囲器の回転軸と同一軸心上に配管され、

ノズルは、給水管に回転可能に結合され、外囲器と一体回転するものであることを特徴とする請求項６に記載のバイオリアクター。

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【発明の詳細な説明】

【０００１】

【発明の属する技術分野】本発明は、細胞塊の培養方法および細胞塊の培養に用いるバイオリアクターに関する。

【０００２】

【従来の技術】バイオリアクターとは、「生物」の細胞塊を培養液中に浮遊させつつその細胞塊の培養を行なう装置である。培養液は、生物の細胞単位で成長させる養液である。この養液には、細胞が生育に必要な栄養素と、ガス、例えば炭酸ガス、酸素などを含有させることにより、細胞の分裂を促し、或いは細胞塊の成長を補助する働きを得ることができる。

【０００３】培養タンク内に充填した培養液に細胞塊を浮遊させながら成長させるに際し、培養液は、流体力学的に絶えず流動させることが求められる。すなわち、培養液を流体力学的に培養タンク内で絶えず流動させる事によって、細胞同士の凝集や細胞凝集塊や組織片へのガスや育成物質の運搬効率が劇的に高まることが立証されている。

【０００４】

【発明が解決しようとする課題】然るに、従来のバイオリアクターは、筒状で、培養液をガスとともに外部から培養タンク内に供給する方式のため、回転する培養タンクには、培養液の供給用配管を接続する必要から構造上の制約をうけることとなり、培養タンクは、定位置で回転する回転軸に取付けられた構造、すなわち、一軸を回転中心として回転させる一軸回転方式のものが殆どであった。

【０００５】ところが、培養タンクを一軸で回転させるだけでは、培養タンク内での培養液の動きに規則性が生じ、とりわけ、回転軸を直角の方向に拡散して行く傾向が強いため、培養タンク内で培養液を充分に流動させることができず、このため、液が劣化し、また、液中に生じた老廃物の除去を行なうことができないという問題点があり、比較的短い時間しか培養を行なうことができないという欠点があった。

【０００６】細胞塊の培養など、バイオテクノロジー技術に関する最近の研究では、培養すべき細胞塊が重力の影響を殆ど受けない空間（所謂模擬無重力空間）を作り出す事が非常に重要である。

【０００７】本発明の目的は、外部から培養液を供給しつつ培養タンクを直交座標の２軸方向に回転させて細胞塊の培養を行なう方法とバイオリアクターを提供することにある。

【０００８】

【課題を解決するための手段】上記目的を達成するため、本発明による細胞塊の培養方法においては、細胞塊を培養する培養タンク内に、互いに直交する２方向の水流を生じさせ、互いに直交する２方向の水流によって、培養タンクの中心付近には均一な流線の球状閉鎖ループが形成され、培養タンクの中心付近に浮遊する細胞塊への重力の影響を殆どなくし、培養液中で中吊りの状態で安定させるものである。

【０００９】また、細胞塊を培養する培養タンク内の培養液には、互いに直交する２方向の水流によって、全体として特定の領域に向かう斜め方向の流れを生じさせ、その水流と、他の領域に回り込んだ水流とを合流させつつ内外多層の循環流を形成させつつ、徐々に各層の培養液を入れ替え、細胞塊に接触する培養液を常に新鮮に保たせるものである。

【００１０】また、本発明によるバイオリアクターにおいては、外部から培養液およびガスが供給される培養タンクを備えたバイオリアクターであって、培養タンクは、培養すべき細胞塊を収容する容器であり、互いに直交する直角座標の２軸をそれぞれ回転中心として回転駆動されるものである。

【００１１】また、培養タンクと、外囲器との組合わせを有するバイオリアクターであって、培養タンクは、培養すべき細胞塊を収容する容器であり、外囲器は、培養タンクを収容する容器であり、培養タンクと、外囲器とは互いに連通して培養液の流通は自在であり、外囲器の回転軸心と、培養タンクの回転軸心とは直交し、培養液およびガスは外囲器内に外部から供給され、培養タンクは、一方向に回転駆動される外囲器内にさらに回転可能に保持され、外囲器と一体回転する駆動源によって回転駆動されるものである。

【００１２】また、ノズルを有し、ノズルは、外囲器と一体に回転しつつ流体を噴出し、培養タンクは、羽根車を有し、ノズルから噴出した流体は羽根車に衝突して培養タンクを回転させるものである。

【００１３】また、培養液の供給用の給水管はノズルに接続され、ノズルより噴出した培養液は、培養タンクを回転させる流体となるものである。

【００１４】また、外囲器は、水平の姿勢に保持されて一方向に回転駆動され、培養タンクは、ピボット軸受によって外囲器の筒体の胴部を横切る方向に回転可能に保持され、培養液の供給する給水管は、外囲器の回転軸と同一軸心上に配管され、ノズルは、給水管に回転可能に結合され、外囲器と一体回転するものである。

【００１５】

【発明の実施の形態】以下に本発明によるバイオリアクターの実施の形態を図によって説明する。図１において、本発明によるバイオリアクター１は、外部から培養液およびガスが供給される培養タンク２を備え、培養タンク２は、互いに直交する直交座標の２軸をそれぞれ回転中心として回転駆動されるものである。

【００１６】本発明によるバイオリアクター１は、培養タンク２と、外囲器３との組合せを有している。培養タンク２は、培養すべき細胞塊を収納する容器であり、外囲器３は、培養タンク２を収納する容器である。培養タンク２と外囲器３とは、互いに連通し、培養液は、培養タンク２と外囲器３間で相互に流通が自在であり、外囲器３から培養タンク２に流入し、あるいは逆に培養タンク２内の培養液は外囲器３内に流出する。

【００１７】培養液Ｃ（細胞の成長に必要な栄養素を含んだ液体、培地ともいう）は、保温槽４内で定温に保温された恒温槽５内に充填されている。恒温槽５内の培養液Ｃは、定量ポンプ６で給水管７Ａに汲み出され、フィルター８を経由して培養液Ｃをろ過し、次いでノズル９から噴出して外囲器３内に供給される。一方、保温槽４には、ガスを充填したガスタンク１０が挿し込まれており、ガスタンク１０内のガスは、一定の温度に制御され、外部から供給されるガスの供給圧力をもって、必要時に、恒温槽５内に供給され、恒温槽５内の培養液Ｃに混合される。ガスは、細胞塊を生存させ、細胞を増殖させるためのガスであり、CO_2：２．５%、N_2：２０%、O_2：２０%を含むガスである。

【００１８】したがって、恒温槽５内にガスが供給されたときには、培養液Ｃは、気液混合流体の形で外囲器３内に供給されるものである。なお、保温槽４は、槽内にヒータ１１を有し、ヒータ１１は、温度制御器１２に制御され、保温槽４内の水は、攪拌ポンプ１３に攪拌されながら一定温度（例えば３７±０．１℃）に保たれる。外囲器３には、排水管７Ｂ、排ガス管７Ｃが接続され、外囲器３内に送り込まれたガスは、排ガス管７Ｃを通して外気に放出される。

【００１９】また、排水管７Ｂは、恒温槽５に接続され、外囲器３内から流出した培養液Ｃは、老廃物を除去し、処理後恒温槽５内に戻される。この実施形態においては、後述するように、ノズル９から噴出する培養液（気液混合培養液）の噴出圧力を培養タンク２の回転駆動源に用いている。

【００２０】図２（ａ）において、外囲器３は、両端が塞がれた筒体であり、軸受１４を介して機枠Ｆに水平の姿勢に回転可能に保持され、筒体の一方の開口を塞ぐ端板１５に固定したプーリ１６と、モータ１７の回転軸に取付けたプーリ１８とが無端ベルト１９によって直結されている。

【００２１】したがって、外囲器３は、モータ１７の駆動により、直交座標の第１軸（水平軸：これをＸ軸とする）を回転軸心として一方向に回転する。培養タンク２は、外囲器３の筒体の胴部に向き合わせに設けたピボット軸受２０に支えられ、外囲器３の筒体の胴部を横切る第２軸（垂直軸：これをＹ軸とする）を回転軸心として回転可能に保持されたものである。

【００２２】すなわち、図３において、培養タンク２は、培養タンク２を開閉する蓋板２１を両端に有する筒体であり、両蓋板２１には、培養タンク２の内外を連通させる連通孔２２が開口され、外囲器３内に供給された培養液Ｃは、フィルター２７を通して連通孔２２から培養タンク２内に流入してその内部を満たし、逆に連通孔２２から外囲器３内に流出して入れ替わる。両蓋板の外面には前記ピボット軸受２０に支持させるピボット２３が取付けられている。ピボット２３は、外囲器３の筒体の胴部内面に向き合わせに設けた軸受に回転可能に支えられる。培養タンク２の筒体の一部周面には、羽根車２４が取付けられている。

【００２３】外囲器３の一方の開口を塞ぐ端板１５は、ブーリ１６に直結された回転端板である。培養液を供給する給水管７Ａは、回転端板１５の回転軸心と同心に配管され、ノズル９は、給水管７Ａとは相互に回転可能に結合され、且つ先端を回転軸心からずらせ、培養タンク２の羽根車２４にむけて屈曲姿勢で配置され、図２（ｂ）に示すように外囲器３の筒体胴部を横切って筒体内壁に取付けられた支え２６に支持されているものである。なお、排水管７Ｂおよび排ガス管７Ｃは、機枠Ｆに固定されたブッシュ２５に支持されて外囲器３内に開口されている。なお、端板１５は、ブッシュ２５の外周に回転可能に支持されている。

【００２４】本発明において、培養すべき細胞塊を培養タンク２内に収容し、培養タンク２は、外囲器３内にセットして外囲器３及び培養タンク２内を培養液で満たし、さらに定量ポンプ６で汲み出した恒温槽５内の培養液Ｃとガスタンク１０内に充填されたガスとを混合し、その気液混合培養液を、給水管７Ａに流入させ、ノズル９より外囲器３内に噴出しつつ細胞塊の培養を開始する。

【００２５】細胞塊の培養に際しては、モータ１７の回転駆動により、水平軸（Ｘ軸）を回転軸心として外囲器３を緩やかに回転させる。ノズル９は、外囲器３と一体に回転しつつ培養液Ｃを噴出し、ノズル９から噴出した培養液Ｃは羽根車２４に衝突し、培養タンク２は、外囲器３のピボット軸受２０に支えられて垂直軸（Ｙ軸）を回転軸心として外囲器３の培養液中で緩やかに回転し、培養タンク２内には、互いに直交する２方向の水流が生じ、互いに直交する２方向の水流は、培養タンクの中心付近には均一な流線の球状閉鎖ループが形成される。

【００２６】培養タンク２内に生ずる培養液の水流の様子を図４を用いて説明する。図４（ａ）において、外囲器３がＸ軸を中心に回転し、同時に培養タンク２がＹ軸を中心に回転すると、培養タンク２内の培養液Ｃには、Ｘ方向の力と、Ｙ方向の力との合力として、図に示すＺ方向の力をうけ、図上、全体として特定の領域、この例では、第４領域から第１領域に向かう斜め方向の流れが生じ、その水流には、他の領域、この例では、第２領域および第３領域に回り込んだ水流が合流して循環流となり、基本的には、図４（ｂ）に示すように多重の層流がそれぞれ球状閉鎖ループを形成し、表層流Ｆｏと、内層流Ｆｉとの間の流れに急激な乱れが生ぜずに同心円の水流を描きつつも培養液の流動にともない、徐々に各層の培養液が入れ替わり、細胞塊に接触する培養液を常に新鮮に保つ。

【００２７】この結果、培養タンク２内を浮遊する細胞塊に掛かる重力は、Ｘ軸、Ｙ軸の回転によって軽減され、培養タンク２内には、疑似無重力空間が形成され、培養タンク２内の中心付近に浮遊する細胞塊は、重力の影響を殆ど受けず、培養液Ｃ中で中吊りの状態となって安定する。

【００２８】以上、実施形態においては、培養タンク２を回転させる動力源としてノズル９から噴出させた培養液（気液混合培養液）Ｃの噴出圧力を利用する例を説明したが、勿論培養液に限らず、その他の循環水あるいは空気またはガスなどの流体を、培養タンクを回転させるための動力に用いることができ、さらには摩擦力を利用して機械的に駆動することも可能である。

【００２９】ただし、磁気および電気のカップリングによる駆動は、細胞に悪影響を及ぼすという説があるため、磁気力や電気力を用いても培養タンクの駆動は可能ではあるものの、培養タンクの駆動に磁気力や電気力を用いるのは避けたほうが望ましい。外囲器の駆動源は、モータに限らず、空気圧又はガス圧を利用して回転駆動することもできる。

【００３０】

【発明の効果】以上のように本発明によるときには、外部から培養液およびガスが供給される培養タンクを、互いに直交する直角座標の２軸をそれぞれ回転中心として回転駆動するため、細胞塊を培養する培養タンク内に、互いに直交する２方向の水流を生じさせ、互いに直交する２方向の水流によって、培養タンクの中心付近には均一な流線の球状閉鎖ループが形成するため、培養タンクの中心付近に浮遊する細胞塊への重力の影響を殆どなくし、培養液中で中吊りの状態で安定させることができる。

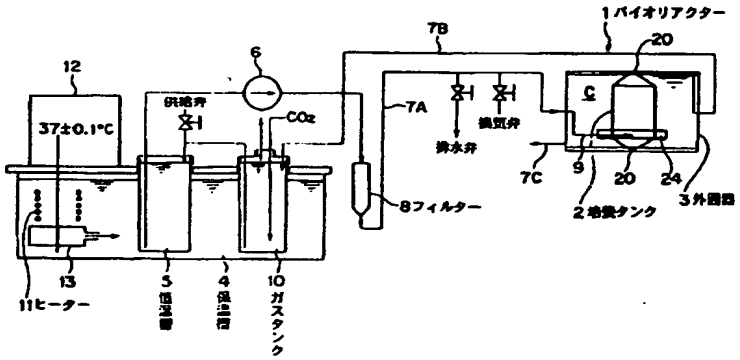
【００３１】また、培養タンクと、外囲器との組合わせを用い、培養タンクと、外囲器とは互いに連通して培養液の流通を自在としたため、外囲器の回転軸心と、培養タンクの回転軸心との組合わせによって、培養タンク内に、無理なく互いに直交する２方向の水流を生じさせることができる。さらに、培養タンクに、羽根車を設けることによって、培養液あるいは、ガスをノズルより噴出させ、その噴出圧力をもって回転する外囲器内で培養タンクをさらに回転させることができる。

【図面の簡単な説明】

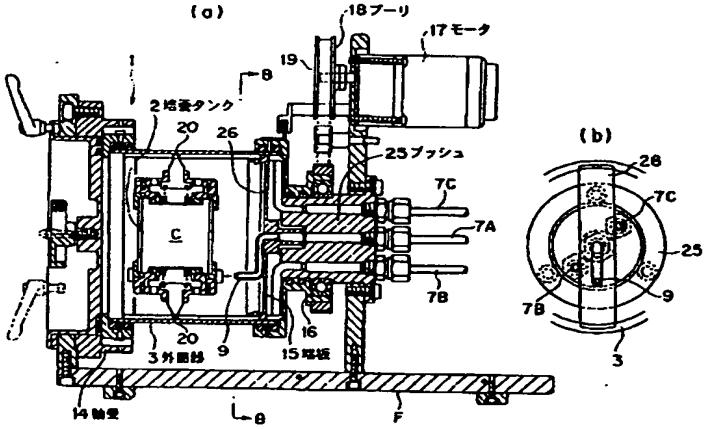
【図１】バイオリアクターの全体の構成を示す図である。

【図２】（ａ）は、バイオリアクターの構造を示す断面側面図、（ｂ）は、（ａ）のＢ－Ｂ線断面図である。
【図３】培養タンクの拡大断面図である。
【図４】（ａ）は、培養タンク内に生ずる循環水流の方向を模式的に示す図、（ｂ）は、表層流と、内層流とが同心状に形成される様子を示す図である。
【符号の説明】
１　バイオリアクター
２　培養タンク
３　外囲器
５　恒温槽
７Ａ　給水管
７Ｂ　排水管
＊７Ｃ　排ガス管
９　ノズル
１４　軸受
１５　端板
１６、１８　プーリ
１７　モータ
２０　ピボット軸受
２２　連通孔
２４　羽根車
２５　ブッシュ
２６　支え
２７　フィルター

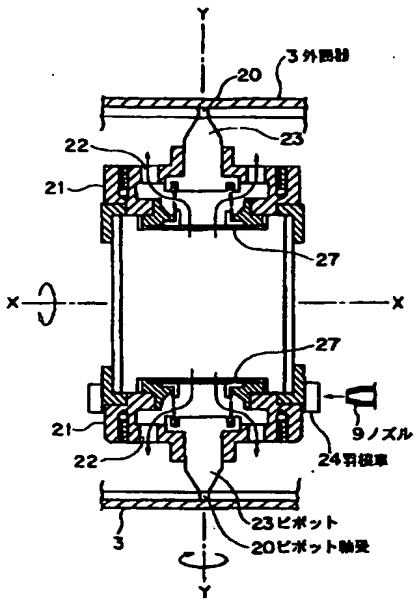
【図１】



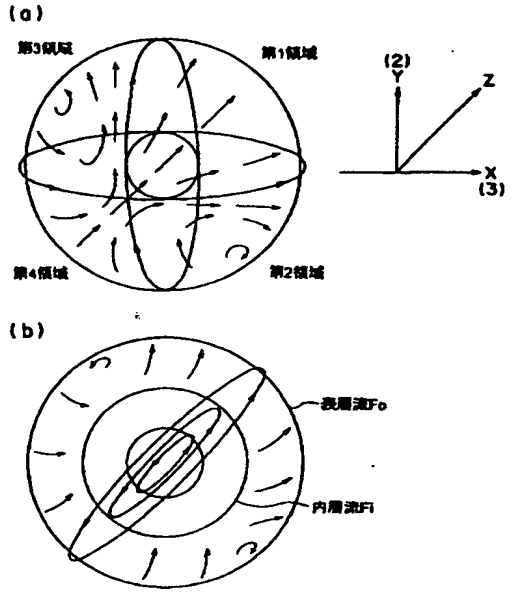
【図２】



【図３】



【図４】



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